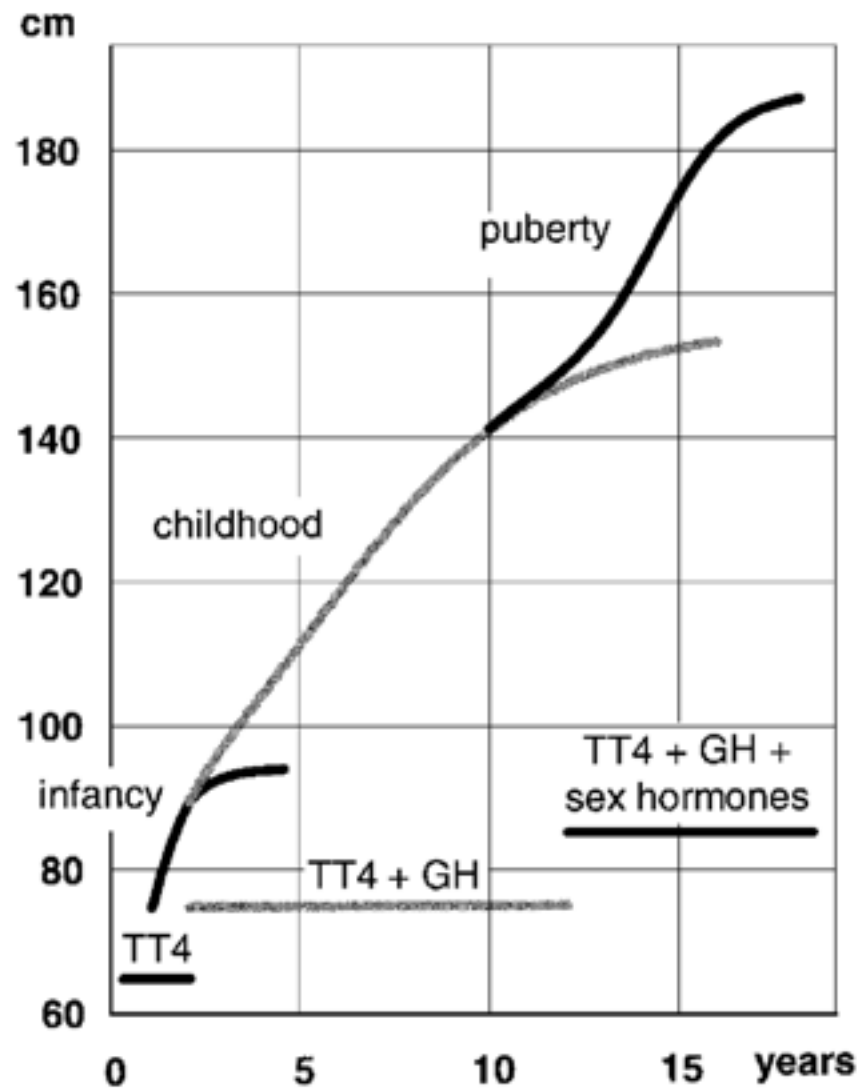
Deficit di GH

06 ottobre 2015

Modello di Karlberg

Difetti di crescita

- Nelle patologie endocrine l'accrescimento staturale rallenta prima o contemporaneamente a quello ponderale
- Nelle patologie da alterato apporto nutrizionale l'accrescimento ponderale rallenta prima di quello staturale

Schweizerbart Science Publishers 2013

Brain

GHRH

SRIF

Pituitary

HESX1
LHX3
LHX4
PROP1
PIT1
SOX3
SOX2

Pituitary development

Ghrelin

Stomach

GH

Liver

IGFBP3

GF1

Bone
Muscle
Fat

anabolic
lipolytic
mineralisation

serum GH (μg/L)

8

6

4

2

fed

fasted

8:00 16:00 0:00 8:00

time of the day (hours)

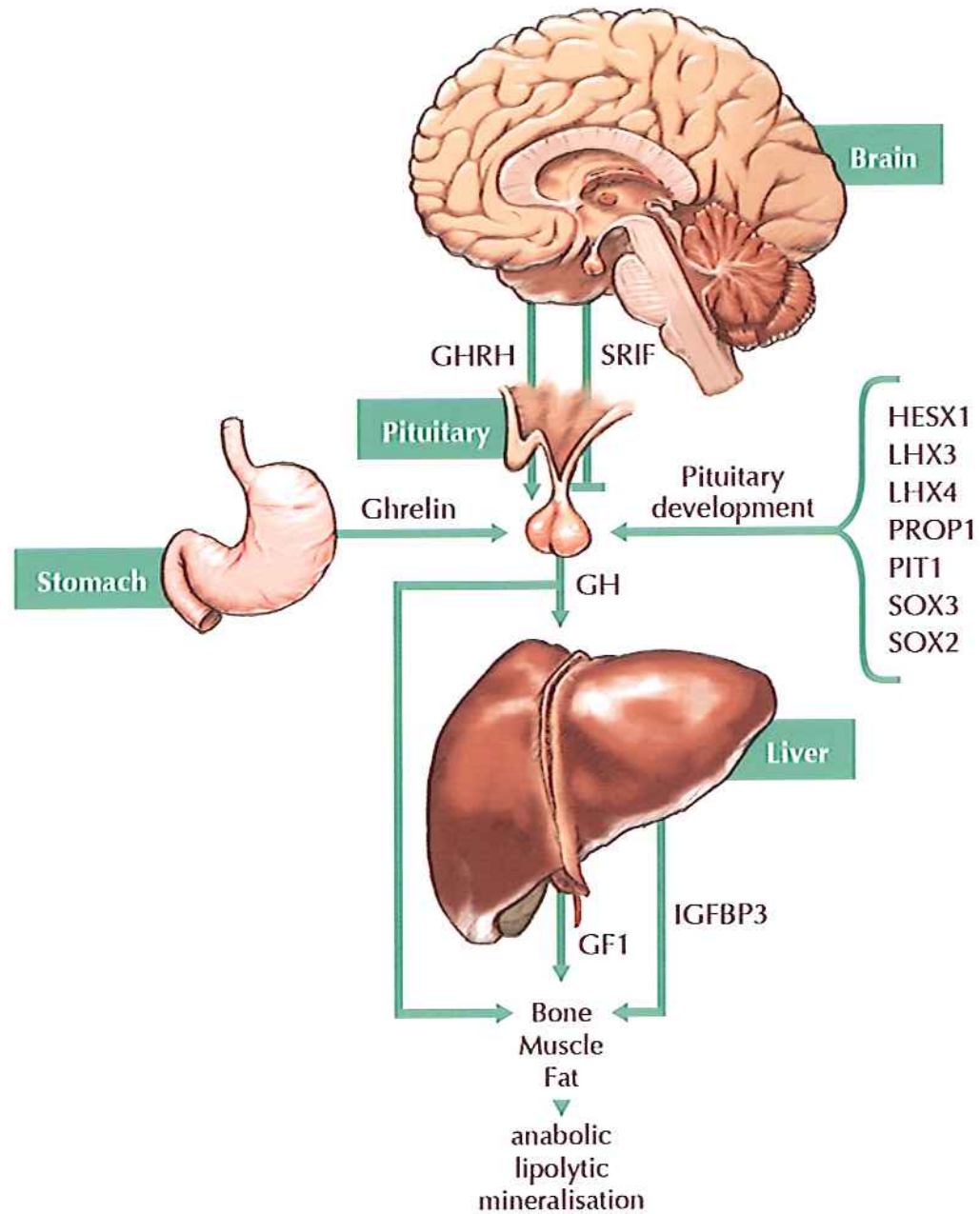
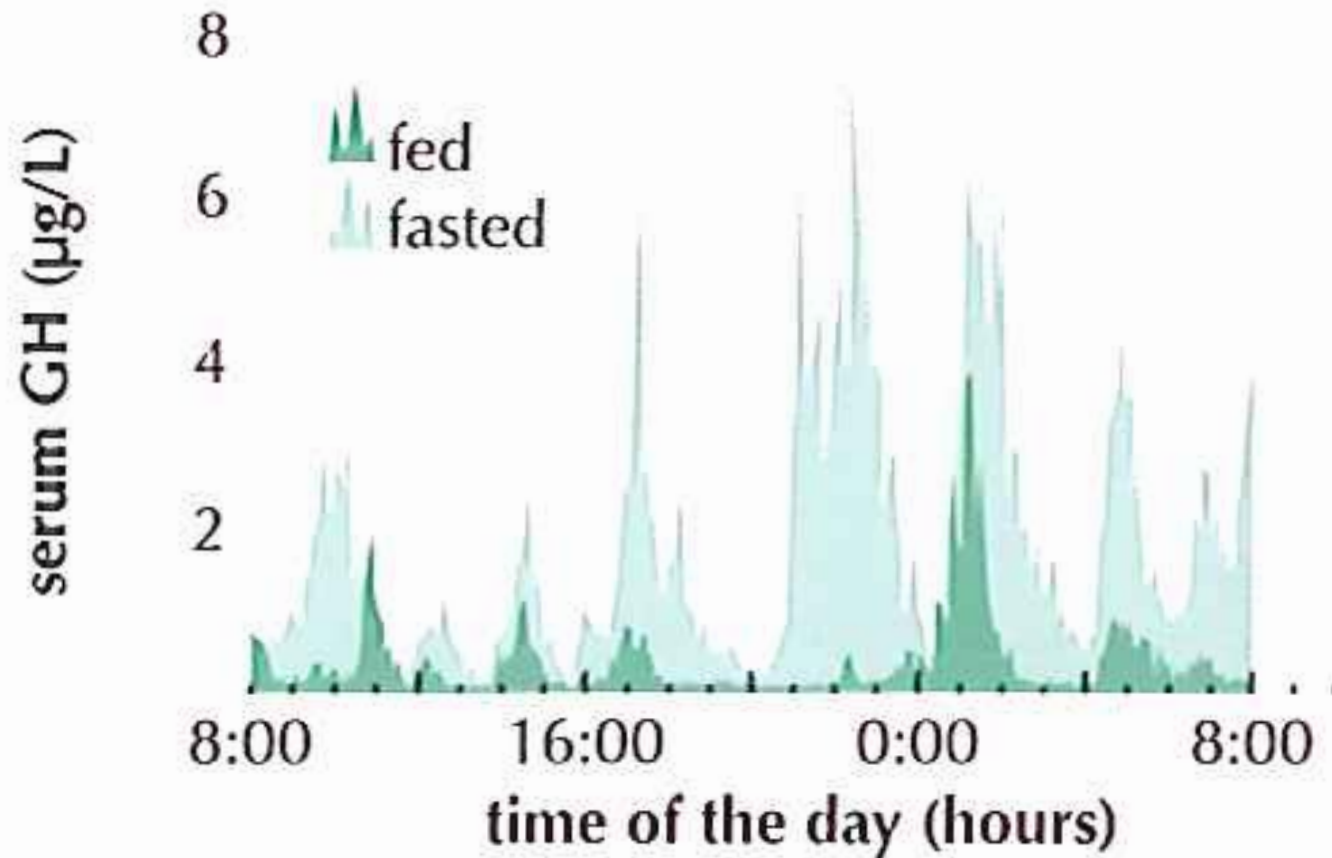



Figure 35: Growth hormone release is pulsatile, and increased when fasted.

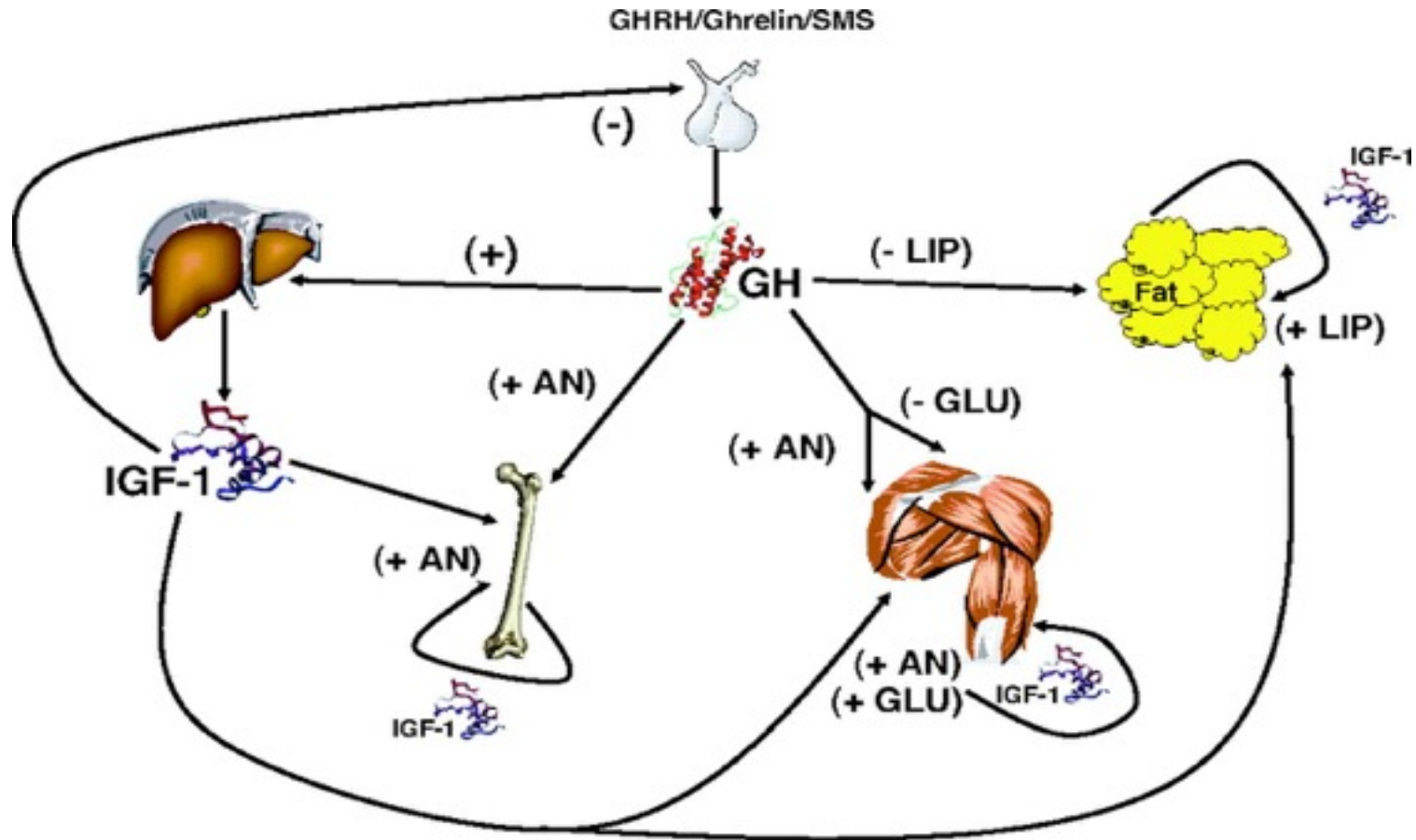
Growth hormone effects are not limited to being a potent mitogen in childhood and adolescence. Also in adults, it stimulates amino acid uptake, protein synthesis, and increases skeletal muscle mass. It has strong lipolytic effects, it promotes insulin secretion and it stimulates the immune system. It also exhibits insulin antagonistic effects as it reduces glucose uptake in the liver and glucose expenditure, and it increases gluconeogenesis.

Growth Hormone

- ✓ La produzione di GH da parte dell'adenoipofisi è regolata dall'ipotalamo attraverso mediatori ad azione stimolatoria, quali il **GHRH** (Growth Hormone Releasing Hormone) ed inibitoria, quali la **somatostatina** e un altro peptide **GHrelina**.

- ✓ Il GH agisce su specifici recettori cellulari inducendo sintesi proteica, lipolisi e antagonizzando l'azione insulinica. Gli effetti sull'accrescimento osseo sono il risultato della mediazione di fattori di crescita specifici tra cui l'**IGF-1** (o somatomedina), sostanza prodotta essenzialmente dal fegato che media gli effetti sull'accrescimento delle epifisi.

FIG. 2. A new somatomedin hypothesis: effects of GH and IGF-I on growth and metabolism

GHRH/Ghrelin/SMS
(-)
IGF-1
(+)
GH
(- LIP)
Fat
(+ LIP)
(+ AN)
(- GLU)
(+ AN)
IGF-1
(+ AN)
(+ AN)
(+ GLU)
IGF-1
IGF-1

Kaplan, S. A. et al. J Clin Endocrinol Metab 2007;92:4529-4535

Cause di Bassa Statura e frequenza % approssimativa

Causa	%
Ritardo costituzionale di crescita e pubertà Bassa statura familiare Bassa statura idiopatica	82
Ritardo intrauterino di crescita	9
Malattie croniche internistiche	6
Cromosomopatie e sindromi mendeliane	1
Osteocondrodisplasie	1
Deficit di GH e altre endocrinopatie	1

Available online at www.sciencedirect.com

Growth Hormone & IGF Research 14 (2004) 185–194

www.elsevier.com/locate/ghir

Review

Is growth hormone stimulation testing in children still appropriate?

Laura M. Gandrud *, Darrell M. Wilson

Division of Pediatric Endocrinology and Diabetes, Stanford University Medical Center, S-302, Stanford University, Stanford, CA 94305-5208, USA

Received 30 July 2003; received in revised form 15 November 2003; accepted 18 November 2003

2004 Gandrud GH test

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The diagnosis of growth hormone deficiency (GHD) historically has relied on measurement of growth hormone (GH) concentrations following stimulation, usually with a non-physiologic provocative agent. Despite the use of more specific GH assays, the peak concentration of GH below which a child is considered GH deficient has risen. We examine the pitfalls associated with GH stimulation tests, specifically, the lack of reliability and accuracy of these tests, and their inability to predict who will benefit from GH therapy. We recommend that GH stimulation tests no longer routinely be used for the diagnosis of GHD in children.

Nota 39

- Determinazione 29 luglio 2010 (GU 18 novembre 2010, n. 270): modifica alla nota AIFA 39 di cui alla determinazione del 26 novembre 2009.

La prescrizione a carico del SSN, su diagnosi e piano terapeutico di centri specializzati, Università, Aziende Ospedaliere, Aziende Sanitarie, IRCCS, individuati dalle Regioni e dalle Province autonome di Trento e Bolzano, è limitata alle seguenti condizioni:

- Parametri auxologici
- Parametri di laboratorio

THE JOURNAL OF PEDIATRICS • www.jpeds.com
ORIGINAL ARTICLES

Hypothalamic-Pituitary Lesions in Pediatric Patients: Endocrine Symptoms Often Precede Neuro-Ophthalmic Presenting Symptoms

Melissa Taylor, MD[1], Ana-Claudia Couto-Silva, MD[1], Luis Adan, MD, PhD[1], Christine Trivin, PhD[2], Christian Sainte-Rose, MD[3], Michel Zerah, MD[3], Dominique Valteau-Couanet, MD[4], François Doz, MD[5], Martin Chalumeau, MD, PhD[6], and Raja Brauner, MD, PhD[1]

(J Pediatr 2012;161:855-63).

Figure 2. Summary diagram of the duration of endocrine signs or symptoms recorded at diagnosis in relation to the neuro-ophthalmic symptom interval in patients with hypothalamic-pituitary lesions associated with neuro-ophthalmic presenting symptoms. The durations of all symptoms and signs are presented as median values in years. The percentages of patients with symptoms are shown for the corresponding symptom interval.

200
175
150
125
100
75
50
25
0
GH
0
24
48
72
96
120
144
168
192
216
mesi

TABLE 7. Approximate height attainment attributed to GH treatment in various diagnostic categories of short stature

Category	n	SD score			GH benefit SD score	cm
		Initial height	PH	FH		
GHD						
<1987	792	−4.2	—	−2.3	1.9	10.1
>1987	4529	−2.9	—	−1.4	1.5	9.0
ISS	413	−2.8	−2.1	−1.7	0.4	2.7
Turner	2211	<−3.0	−3.3	−2.3	1.0	5.8
SGA	16[a]	−2.7	−1.7	−1.7	1.0	6.0
	70[b]	−2.9	−2.4	−2.0	0.4	2.4
	40[c]	−2.6	−2.2	−2.2	—	—

[a] Ranke and Lindberg (71). Received GH at a dose of 0.7 IU/kg·week for an average of 4.7 yr.

[b] Coutant *et al.* (72). Received GH at a dose of 0.4 IU/kg·week for an average of 4.6 yr.

[c] Coutant *et al.* (72). Untreated control group.

Comportamento attuale

Iter diagnostico nelle basse stature e nel deficit di GH in particolare

- Anamnesi
- Esame obiettivo
- Valutazione auxologica: statura, proporzioni corporee e velocità di crescita
- Valutazione età ossea
- Esami di routine per escludere patologie d'organo o di apparato: esami di funzionalità renale ed epatica, ATG, (IgA), esame parassitologico feci, FT4, TSH
- Cariotipo (femmine)

- Dosaggio IGF-I e/o IGFBP-3 (effettori periferici)
- Valutazione della secrezione di GH
  - stimolo farmacologico (o fisiologico) (ripetuto se patologico)
  - concentrazione integrata (nella notte o nelle 24 ore)
- Determinazione della eventuale patologia alla base del difetto di GH (RM) e di altri deficit associati

TEST DI PROVOCAZIONE (1)

- Carico con arginina
- Carico con insulina
- Carico con Clonidina
- Carico con Glucagone: se paziente < 5 anni e/o < 20 kg;

TEST DI PROVOCAZIONE (3)

Come interpretarli:

Se il picco di GH e':

- > 8 ng/ml: **NORMALE**, non c'e' deficit di GH;
- 5 - 8 ng/ml: **DEFICIT PARZIALE**;
- < 5 ng/ml: **DEFICIT DI GH**

attenzione al BMI

Deficit di ormone della crescita (GHD)

Il quadro clinico è variabile a seconda che:

- Il deficit sia isolato o associato a defcit di altre tropine ipofosarie
- L'entità del deficit sia totale o parziale
- Il deficit sia primitivo o secondario a patologie organiche intra- o extracraniche.

Deficit di ormone della crescita

frequenza di circa 1/4000

forma completa o classica

bassa statura (< -2 DS per l'età)

velocità di crescita ridotta (< 25° PC per età ossea)

proporzioni corporee normali, peso lievemente superiore a quello normale per la statura, viso a bambola, aumento grasso pubico

maturazione ossea ritardata (> 2 aa)

secrezione anomala di ormone della crescita (almeno due stimoli con picco di GH < 10ng/ml)

bassi livelli di IGF-I e/o IGFBP-3

non segni di altre malattie significative

non evidente privazione affettiva

assenza di altre cause per lo scarso accrescimento

Forme gravi: storia di ipoglicemia perinatale, anemia ipocromica, di convulsioni, micropene con testicoli in sede

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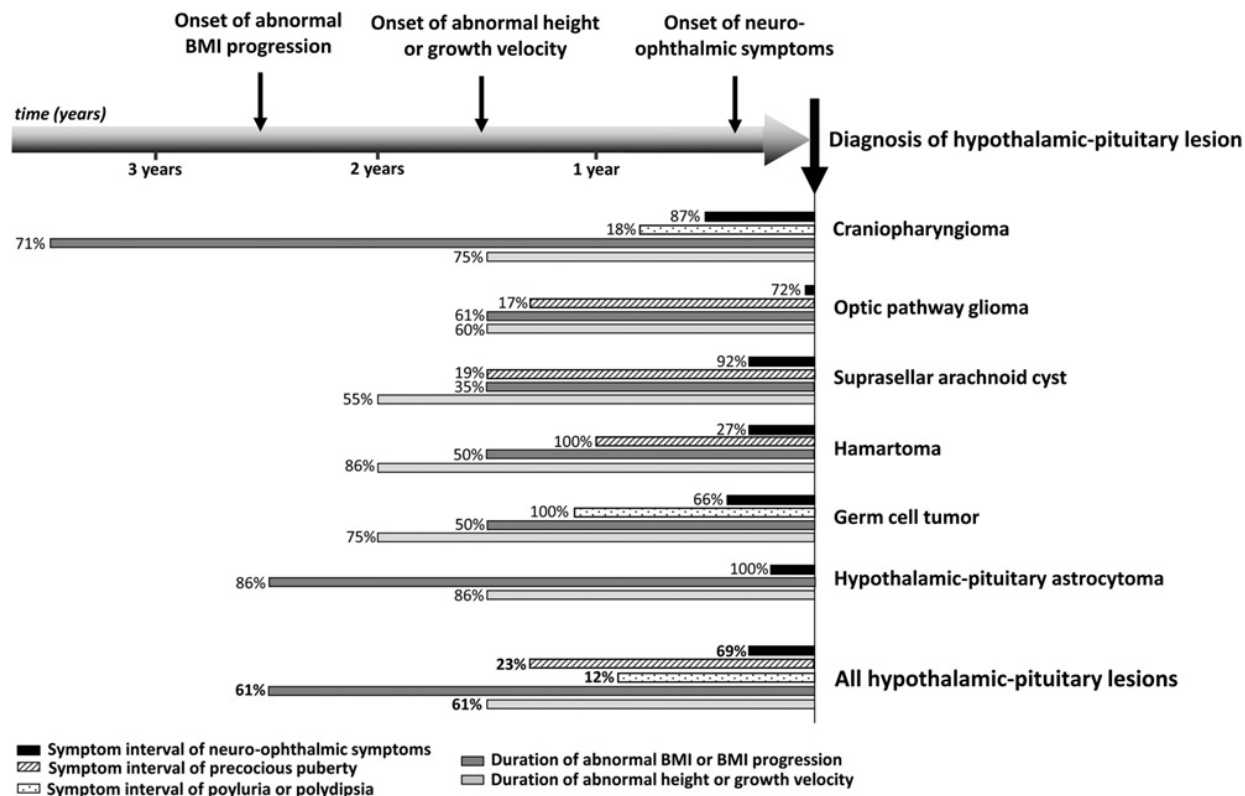
Figure 1. Summary diagram of the symptom intervals of neuro-ophthalmic symptoms and endocrine signs or symptoms recorded at diagnosis in patients with hypothalamic-pituitary lesions. The durations of all symptoms and signs are presented as median values in years. The percentages of patients with symptoms are shown for the corresponding symptom interval.

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